

Amendments to the Claims

1. (Original) A cobalamin derivative

- (a) having no binding affinity or low binding affinity to transcobalamin II and
- (b) retaining activity as a vitamin B12 substitute.

2. (Original) The cobalamin derivative according to claim 1

- (a) having less than 20% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
- (b) retaining more than 2% of the activity as a vitamin B12 substitute in a growth assay.

3. (Original) The cobalamin derivative according to claim 1

- (a) having less than 10% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
- (b) retaining more than 10% of the activity as a vitamin B12 substitute in a growth assay.

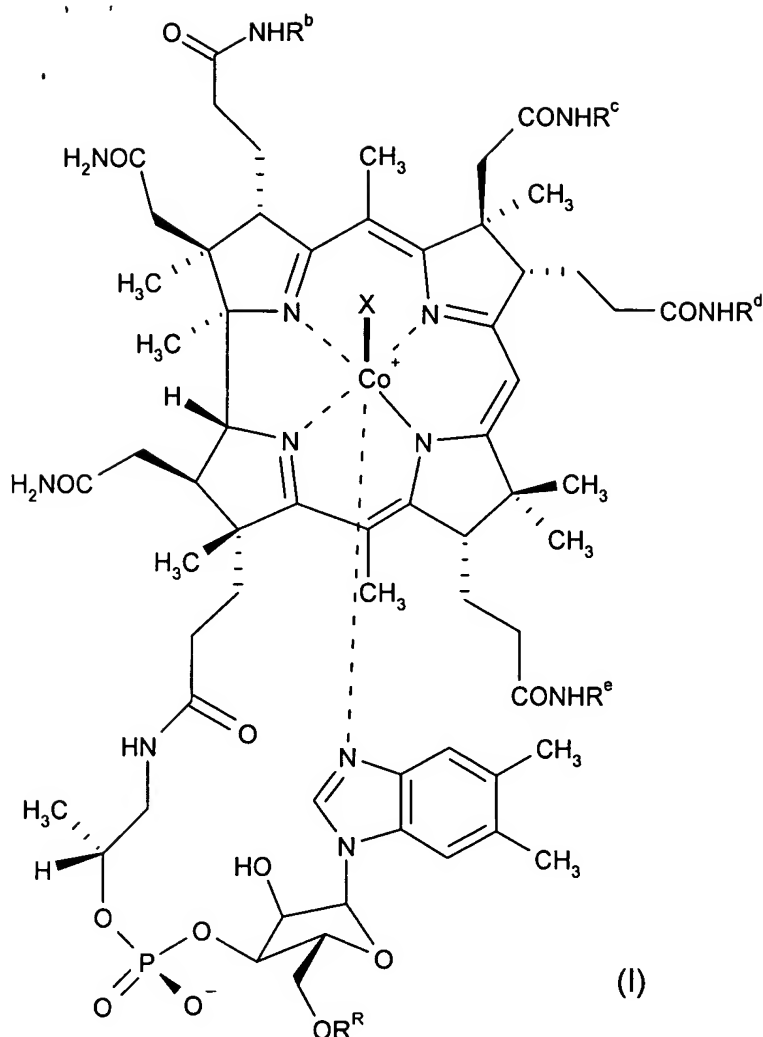
4. (Original) The cobalamin derivative according to claim 1

- (a) having less than 5% of binding affinity to transcobalamin II when compared to the binding affinity of non-modified cobalamin in a binding test, and
- (b) retaining more than 10% of the activity as a vitamin B12 substitute in a growth assay.

5. (Currently amended) The cobalamin derivative according to ~~anyone of claims 1 to 4~~ claim 1 carrying a therapeutic and/or diagnostic agent.

6. (Currently amended) The cobalamin derivative according to ~~anyone of claims 1 to 5~~ claim 1 carrying a radioactive metal.

7. (Currently amended) The cobalamin derivative according to ~~anyone of claims 1 to 6~~ claim 1 of formula (I)



wherein

R^b , R^c , R^d and R^e , independently of each other, are a spacer-chelator group, an antibiotic or antiproliferative therapeutic agent, a sterically demanding organic group with 4 to 20 carbon atoms, or hydrogen;

R^R is a spacer-chelator group or an antibiotic or antiproliferative therapeutic agent, each connected through a linker Z, or hydrogen;

with the proviso that at least three of the residues R^b , R^c , R^d , R^e and R^R are hydrogen and at least one of the residues R^b , R^c , R^d and R^e is different from hydrogen;

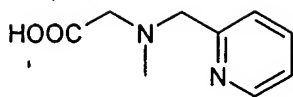
X is a monodentate ligand; and

the central cobalt (Co) atom is optionally in the form of a radioactive isotope.

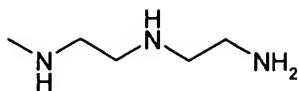
8. (Original) The cobalamin derivative according to claim 7 wherein R^e is hydrogen.

9. (Currently amended) The cobalamin derivative according to claim 7 ~~or 8~~ wherein the spacer-chelator group comprises
a spacer, which is an aliphatic chain of 2 to 10 carbon atoms, wherein one or two carbon atoms may be replaced by nitrogen and/or oxygen atoms and the aliphatic chain may be substituted by hydroxy, oxo or amino, and
a chelator, which is a compound having two, three or more donor atoms selected from nitrogen, oxygen and sulfur in a distance such as to bind to a metal atom, and optionally a metal atom.

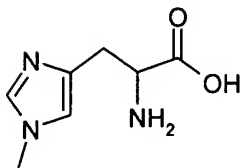
10. (Original) The cobalamin derivative according to claim 9 wherein the chelator is selected from the chelators of formula (II) to (IX),



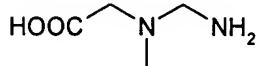
(II)



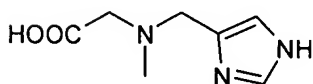
(III)



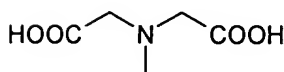
(IV)



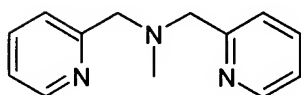
(V)



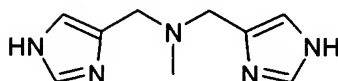
(VI)



(VII)



(VIII)



(IX)

wherein carboxyl groups may be present as esters.

11. (Currently amended) The cobalamin derivative according to ~~anyone of claims 6 to 10~~ claim 6 wherein the radioactive metal is ^{94m}Tc , ^{99m}Tc , ^{188}Re , ^{186}Re , ^{111}In , ^{90}Y , ^{64}Cu , ^{67}Cu or ^{177}Lu .

12. (Currently amended) The cobalamin derivative according to ~~anyone of claims 7 to 11~~ claim 7 wherein X is cyano, methyl, hydroxy, aquo or a 5'-deoxyadenosyl group.

13. (Original) The cobalamin derivative according to claim 12 wherein X is cyano.

14. (Currently amended) The cobalamin derivative according to ~~anyone of claims 7 to 12~~ claim 7 wherein the central cobalt atom is the radioisotope ^{57}Co or ^{60}Co .

15. (Original) The cobalamin derivative according to claim 10 wherein R^b is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 2 to 4 carbon atoms, and the chelator is of formula (II), wherein the group COOH is optionally in the form of an ester; R^c , R^d , R^e and R^R are hydrogen; and X is cyano.

16. (Original) The cobalamin derivative according to claim 15 wherein R^b is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 4 carbon atoms, and the chelator is of formula (II), wherein the group COOH is in the form of the ethyl ester; R^c , R^d , R^e and R^R are hydrogen; and X is cyano.

17. (Original) The cobalamin derivative according to claim 10 wherein R^d is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 3 carbon atoms, and the chelator is of formula (II), wherein the group COOH is optionally in the form of an ester; R^b , R^c , R^e and R^R are hydrogen; and X is cyano.

18. (Original) The cobalamin derivative according to claim 10 wherein R^b is a spacer-chelator group optionally carrying a metal atom, the spacer is an aliphatic chain of 2 carbon atoms, and the chelator is of formula (III); R^c , R^d , R^e and R^R are hydrogen; and X is cyano.

19. (Currently amended) A pharmaceutical composition comprising a cobalamin derivative according to ~~anyone of claims 1 to 18~~ claim 1.

20. (Currently amended) A method of diagnosis of a neoplastic disease or an infection by microorganisms in a mammal comprising

- (a) exposing the mammal suspected of being inflicted by a neoplastic disease or an infection to a period of a vitamin B12 – free diet, and
- (b) subsequently applying a cobalamin derivative according to ~~anyone of claims 1 to 18~~ claim 1 carrying a diagnostic agent.

21. (Currently amended) A method of treatment of a mammal suffering from a neoplastic disease or an infection by microorganisms comprising

- (a) exposing the mammal in need of treatment to a period of a vitamin B12 – free diet, and
- (b) subsequently applying a cobalamin derivative according to ~~anyone of claims 1 to 18~~ claim 1 carrying a therapeutic agent.

22-25. (Cancelled)

26. (New) The method of claim 20, wherein the cobalamin is effective in cancer imaging.

27. (New) The method of claim 21, wherein the cobalamin is effective in cancer imaging.